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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER

18N2/0825

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ART UNIT	PAPER NUMBER
1818	25

DATE MAILED: 08/25/97

[illegible] a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 3/1/96, 12/9/96, 12/13/96, & 5/21/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-3, 5-7, 9-26, 28-38, & 40-80 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☑ Claim(s) 1-3, 5-7, 9-26, 28-38, & 40-80 is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40517

The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1819.

Claims 1, 16, 17, 32, 44, and 52 are amended as requested in the after-final amendment filed 9 December 1996, and new claims 57-80 have been added as requested in the amendment filed 21 May 1997. Claims 1-3, 5-7, 9-26, 28-38, and 40-80 are now pending in the application and have been examined.

Table 6 on page 25 appears to contain an error - there are two columns in the Table with data for "in" (intranasal) administration, while the same data presented in Table 7 of the 5,643,578 patent (column 11) indicates that the data column showing 10/12 survival was for "iv" (intravenous) administration.

All grounds for rejection of claims stated in previous Office actions which are not re-stated below are withdrawn.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 6, 7, 25, 26, and 52 rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 14, 15, 17, and 18 of prior U.S. Patent No. 5,643,578. This is a double patenting rejection.

The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper

timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5, 9-24, 28-38, 40-51, 53-61, and 75-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 5,643,578. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass overlapping subject matter.

Claims 2, 5-9, 10, 12, 18, and 34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite in it dependence on canceled claim 4.

Claim 12 is indefinite in its recitation of "the mammal," as there is no antecedent basis for the recited mammal in the series of claims on which claim 12 depends.

Claims 2, 18, and 34 are indefinite because the meaning of the term "nonretroviral" is not clear; e.g., it is unclear whether the term "nonretroviral" in the claim refers to a specific type of retrovirus (type number nine?) or implies that the promoter is not of retroviral origin. If the intended meaning is the latter, amending the claim to state that the promoter is not of retroviral origin would obviate this ground of rejection.

Claims 1-3, 5, 6, 11-25, 30-37, 42, 43, 52-58, 61, and 75 are rejected under 35 U.S.C. § 112, first paragraph, because the specification is enabling for the claimed invention wherein the antigen is an influenza virus hemagglutinin (HA) protein, but it does not provide enablement for the claimed invention wherein the recited DNA transcription unit encodes any other type of protein.

Applicants' demonstration that protective immunity against infection by influenza virus can be elicited in three different animal species by administration of an expression vector encoding either of two different influenza virus HA proteins is evidence that one skilled in the art would not have to perform undue experimentation to successfully practice the claimed invention using an expression vector encoding an influenza HA protein. The claims broadly encompass a vast number of antigens of unknown activity, but the specification provides insufficient guidance regarding which genes encoding antigens of infectious agents can be administered according to the claimed invention to successfully confer protective immunity as was achieved using vectors encoding influenza virus HA protein. At the time the application was filed, it was well-known by those skilled in the art that it is impossible to predict whether an untested antigen of an infectious pathogen will elicit a protective immune response in a given type of animal (see Zinkernagel, in Fundamental Immunology, 3rd Ed., p. 1222, for example). One skilled in the art would also have recognized that results observed in animal model systems following testing of a DNA expression vector-based agent are not predictive of outcome or efficacy in applications in other species of animal or in humans, due to differences in anatomy, cell biology, genetics, and immunology between different types of animals, and between the animal models and humans (Ledley, p. 79).

Example 10 shows that administration of a vector encoding a rotavirus VP7 protein stimulates production of antibodies and

activates T-cells against the VP7 protein, and Dr. Robinson's second declaration states that administration of a vector encoding a measles virus HA or F protein to mice and rabbits stimulates production of antibodies against said proteins. One skilled in the art at the time the application was filed would not have regarded these studies as convincing evidence of elicitation of protective immunity, because it was recognized by those skilled in the art that elicitation of a humoral or cellular immune response is not correlated with protective immunity (Kuby et al., left column; Hoffenbach et al., p. 459; Butini et al.). Moreover, in view of the unpredictability of the claimed invention in animals as discussed above, even if data were provided showing that vectors encoding said viral proteins elicit a protective immune response in the treated animals, there is no evidence in the specification or in the scientific literature that would convince one skilled in the art that such a result is predictive that other proteins of the same viruses will also elicit protective immunity, or that administration of said vectors will also elicit protective immunity against rotavirus or measles virus in other animals and in humans.

Examples 11-15 describe making and administering DNA vectors encoding antigens of SIV and HIV, but Applicants have not provided convincing evidence that such treatment elicits protective immunity against SIV or HIV in the treated subject. Dr. Robinson's first declaration teaches that administration of plasmids encoding SIV env protein to macaques caused viral loads to be reduced to chronic levels more rapidly than occurs in control animals, but the method failed to protect the treated animals from SIV infection and death by AIDS. That the operation of the claimed method is highly unpredictable is also reflected in the fact that, while the gene gun method of DNA administration was most effective in eliciting protection against influenza virus, all of the macaques treated by the gene gun method were in

the group which died by one year after SIV challenge.

In view of the high level of unpredictability of the claimed invention, as discussed above, and given that the specification only provides examples demonstrating successful operation of the claimed invention wherein the antigen is an influenza virus HA protein, and given the lack of guidance in the specification regarding how to successfully use the claimed invention wherein the vector encodes any other antigen, undue experimentation would have been required by one skilled in the art at the time the application was filed to use the claimed invention except wherein the antigen encoded by the expression vector is an influenza virus HA protein.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and use the invention. The rejected claims broadly recite administering, to any mammal or vertabrate, a vector encoding any protein from SIV or HIV, such as the env protein, to elicit protective immunity. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. At the time the application was filed, those skilled in the art recognized that it is impossible to predict whether an untested antigen of an infectious pathogen will elicit a protective immune response in a given type of animal, and that results observed in animal model systems following administration of a DNA expression vector

cannot be assumed to be predictive of outcome or efficacy in applications in other species of animal or in humans, as discussed above. With particular regard to immunity against HIV, Haynes et al. teach that the immune correlates for protection against HIV are not known, that there is no animal model that mirrors human HIV infection, and that current animal models for SIV or HIV infection do not develop AIDS symptoms or anti-HIV immune responses analogous to those of HIV-infected humans, so that it is impossible to determine whether observation of a given immune response to an immunodeficiency virus vaccine in an animal model indicates that the tested vaccine actually confers protection against the virus in a human (p. 1280. left column). In support of this view, the recent disclosure by Weiner et al. (see Weiss) that protective immunity against HIV could be elicited in chimpanzees by administering DNA encoding 4 different HIV genes was met with skepticism by those skilled in the art, who noted that "many other AIDS vaccines have looked similarly promising at the same early stage of development, only to fail in humans." Those skilled in the art would reasonably regard Applicants' results obtained with anti-SIV vaccine in macaques described in Dr. Robinson's first declaration as having even less correlation with outcome in humans than the results obtained by Weiner et al., since the immune system of chimps is more similar to that of humans. Accordingly, one skilled in the art would not regard Applicants' results obtained with anti-SIV vaccine in macaques as being correlative with outcome or efficacy of a similar vaccine in a human.

Given the breadth of the claims, which encompass vectors comprising any type of promoter and genes encoding any SIV or HIV protein, given the unpredictability of the operation of the claimed invention and the lack of correlative examples as discussed above, one skilled in the art would reasonably have considered that at the time the application was filed undue

experimentation would have been required to use the claimed invention to succesfully elicit protective immunity against SIV or HIV infection in an animal or human.

Claims 9, 10, 28, 29, 40, 41, 44-51, and 62-74 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 57, 59, 75, 76, and 77 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Townsend et al., who disclose an expression vector comprising a promoter operably linked to a DNA sequence encoding H1 hemagglutinin of influenza virus, and show that said vector operates in a transfected mammalian cell to direct production of said H1 hemagglutinin protein. The ability of said vector to function to direct production of H1 hemagglutininin in a cell of a mammal inoculated with said vector is considered an inherent property of said vector.

No claims are allowed.

The Declarations of Dr. Robinson filed 3/1/96 and 12/13/96, the Declaration of Dr. Rosenberg filed 9/12/96, are insufficient to overcome the rejections of the claims based upon 35 U.S.C. § 112, first paragraph, for the reasons presented above.

Applicant's arguments in the amendments filed 12/9/96 and 5/21/97, have been fully considered but they are not deemed to be persuasive, for the reasons discussed above.

General Information Regarding Further Correspondence

Any inquiry concerning this or earlier communications from the examiner should be directed to Dr. Charles Rories, Group 1800, Art Unit 1819, at telephone number (703)-308-1120. The examiner can normally be reached from 7:30 AM to 5:00 PM on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached at (703)-308-2035.

Papers related to this application may be submitted to Art Unit 1819 in Crystal Mall I by facsimile transmission to telephone number (703)-305-4242 or (703)-305-3014. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Any inquiry of a general nature or relating to the status of this application, should be directed to the Group 1800 receptionist, at telephone number (703)-308-0196.

18 August 1997

Charles C. P. Rories

Charles C. P. Rories
Patent Examiner
Art Unit 1819